CLAIMS

We claim:

1. A non-human mammal comprising a modified endogenous gene, wherein said endogenous gene is selected from the group consisting of a gene or sequence encoding an ion-channel, a G-protein coupled receptor (GPCR), an immunoglobulin, a growth factor, an enzyme, or a milk protein.

2. A mammal according to claim 1 wherein said mammal is a farm animal.

3. A mammal according to claim 2 wherein said farm animal is selected from the group consisting of cattle, sheep, pigs, horses and goats.

4. A mammal according to claim 1 wherein said mammal is selected from the group consisting of mice, rats, rabbits , guinea pigs, hamsters and gerbils.

5. A mammal according to claim 1 wherein said milk protein gene is a lactoglobulin gene.

6. A mammal according to claim 5 wherein said lactoglobulin gene is the α-lactoglobulin gene or the β-lactoglobulin gene.

7. A mammal according to claim 6 wherein said modified α-lactoglobulin gene or β-lactoglobulin gene does not encode any phenylalanine residues.

8. A mammal according to claim 1 wherein said endogenous gene is disrupted by deletion of at least one nucleotide.

9. A mammal according to claim 1 wherein said endogenous gene is disrupted by an insertion sequence.

10. A mammal according to claim 9 wherein said insertion sequence is a polylinker sequence.

11. A mammal according to claim 9 wherein said insertion sequence is a reporter gene.

12. A mammal according to claim 11 wherein said reporter gene is selected from the group consisting of a luciferase gene, a β-galactosidase gene and green fluorescent protein (GFP), blue fluorescent protein (BFP), red fluorescent protein (RFP) and yellow fluorescent protein (YFP).

13. A mammal according to claim 9 wherein said insertion sequence is selected from the group consisting of a gene encoding human lysozyme, human growth hormone, human serum albumin, human globin, a human immunoglobulin, and a human enzyme.

14. A mammal according to claim 12 wherein said human enzyme is α-1 antitrypsin.

15. A mammal according to claim 12 wherein said human enzyme is anti-thrombin III.

16. A mammal according to claim 12 wherein said human enzyme gene does not encode any phenylalanine residues.

17. A mammal according to claim 9 wherein said insertion sequence is selected from the group consisting of a human gene under control of its endogenous promoter, a modified endogenous regulatory element for an endogenous gene, a transcriptional regulation cassette and a dimerizing sequence.

18. A mammal according to claim 17 wherein said endogenous regulatory element is disrupted by deletion of at least one nucleotide.

19. A mammal according to claim 17 wherein said regulatory element is disrupted by an insertion sequence.

20. A mammal according to claim 1 wherein said enzyme is a sugar transferase enzyme.

21. A mammal according to claim 20 wherein said sugar transferase enzyme is α-galactosyl transferase.

22. A mammal according to claim 21 wherein said α-galactosyl transferase gene is disrupted by deletion of at least one nucleotide.

23. A mammal according to claim 21 wherein said α-galactosyl transferase gene is disrupted by an insertion sequence.

24. A mammal according to claim 23 wherein said insertion sequence is a hormone receptor gene.

25. A mammal according to claim 23 wherein said insertion sequence is a viral receptor gene.

26. A mammal according to claim 23 wherein said insertion sequence is a G-protein coupled receptor gene.

27. A primate comprising a modified endogenous gene.

28. A primate according to claim 27 wherein said endogenous gene is disrupted by deletion of at least one nucleotide.

29. A primate according to claim 27 wherein said endogenous gene is disrupted by an insertion sequence.

30. A primate according to claim 29 wherein said insertion sequence is a human therapeutic gene.

31. A primate according to claim 29 wherein said insertion sequence is a human antibody gene.